

WHAT IS CLAIMED IS:

1. A therapeutic composition for treating a wound, comprising a therapeutically effective amount of an isolated, purified, recombinant heparanase, said heparanase being substantially free of contaminants, and a pharmaceutical carrier adapted for application to the wound.

2. The composition of claim 1, wherein said recombinant heparanase includes a polypeptide having heparanase catalytic activity as set forth in SEQ ID Nos: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity.

3. The composition of claim 2, wherein said recombinant heparanase includes a polypeptide at least 60% homologous to SEQ ID NOs: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity, as determined with the Smith-Waterman algorithm, using the Bioaccelerator platform developed by Compugene (gapop equals 10.0, gapext equals 0.5, matrix: blosum 62).

4. The composition of claim 2, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide as set forth in any of SEQ ID NOs: 9, 13, 42 or 43.

5. The composition of claim 4, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide at least 60% identical with SEQ ID NOs: 9, 13, 42 or 43 as determined using the Bestfit procedure of the DNA sequence analysis software package developed by the Genetic Computer Group (GCG) at the University of Wisconsin (gap creation penalty equals 12, gap extension penalty equals 4).

6. The composition of claim 1, wherein said heparanase has a concentration in a range of from about 0.005 microgram per 1 cm² to about 50 microgram per 1 cm² of wound area.

7. The composition of claim 6, wherein said heparanase has a concentration in a range of from about 0.5 microgram per 1 cm² to about 5 microgram per 1 cm² of wound area.

8. The composition of claim 1, wherein said heparanase is present in a concentration in a range of from about 10 micrograms to about 150 micrograms per dose.

9. A method of inducing or accelerating a healing process of a wound, the method comprising administering to the wound a therapeutically effective amount of an isolated, purified heparanase, said isolated, purified heparanase being substantially free of contaminants, so as to induce or accelerate the healing process of the wound.

10. The method of claim 6, wherein said wound is selected from the group consisting of an ulcer, a burn, laceration, a surgical incision, necrosis and a pressure wound.

11. The method of claim 10, wherein said ulcer is a diabetic ulcer.

12. The method of claim 6, wherein said heparanase is recombinant.

13. The method of claim 12, wherein said recombinant heparanase includes a polypeptide having heparanase catalytic activity as set

forth in SEQ ID Nos: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity.

14. The method of claim 9, wherein said recombinant heparanase includes a polypeptide having heparanase catalytic activity at least 60% homologous to SEQ ID NOs: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity, as determined with the Smith-Waterman algorithm, using the Bioaccelerator platform developed by Compugene (gapop equals 10.0, gapext equals 0.5, matrix: blosum 62).

15. The method of claim 9, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide as set forth in any of SEQ ID NOs: 9, 13, 42 or 43.

16. The method of claim 15, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide at least 60% identical with SEQ ID NOs: 9, 13, 42 or 43 as determined using the Bestfit procedure of the DNA sequence analysis software package developed by the Genetic Computer Group (GCG) at the University of Wisconsin (gap creation penalty equals 12, gap extension penalty equals 4).

17. The method of claim 6, wherein said heparanase is contained in a pharmaceutical composition adapted for topical application.

18. The method of claim 17, wherein said pharmaceutical composition is selected from the group consisting of an aqueous solution, a gel, a cream, a paste, a lotion, a spray, a suspension, a powder, a dispersion, a salve and an ointment.

19. The method of claim 17, wherein said pharmaceutical composition includes a solid support.

20. The method of claim 17, wherein said heparanase has a concentration in a range of from about 0.005 microgram per 1 cm² to about 50 microgram per 1 cm² of wound area.

21. The method of claim 20, wherein said heparanase has a concentration in a range of from about 0.5 microgram per 1 cm² to about 5 microgram per 1 cm² of wound area.

22. The method of claim 9, wherein said heparanase is present in a concentration in a range of from about 10 micrograms to about 150 micrograms per dose.

23. A pharmaceutical composition for inducing or accelerating a healing process of a wound, the pharmaceutical composition comprising, as an active ingredient, an isolated, purified, recombinant heparanase and a pharmaceutically acceptable carrier for topical application of the pharmaceutical composition, wherein said recombinant heparanase includes a polypeptide having heparanase catalytic activity as set forth in SEQ ID Nos: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity.

24. The composition of claim 23, wherein said recombinant heparanase includes a polypeptide at least 60% homologous to SEQ ID NOs: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity, as determined with the Smith-Waterman algorithm, using the Bioaccelerator platform developed by Compugene (gapop equals 10.0, gapext equals 0.5, matrix: blosum 62).

25. The composition of claim 23, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide as set forth in any of SEQ ID NOs: 9, 13, 42 or 43.

26. The composition of claim 25, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide at least 60% identical with SEQ ID NOs: 9, 13, 42 or 43 as determined using the Bestfit procedure of the DNA sequence analysis software package developed by the Genetic Computer Group (GCG) at the University of Wisconsin (gap creation penalty equals 12, gap extension penalty equals 4).

27. The composition of claim 23, packed and identified for treatment of wounds.

28. The composition of claim 23, wherein said pharmaceutical composition is selected from the group consisting of an aqueous solution, a gel, a cream, a paste, a lotion, a spray, a suspension, a powder, a dispersion, a salve and an ointment.

29. The composition of claim 28, wherein said pharmaceutical composition includes a solid support.

30. The composition of claim 23, wherein said heparanase has a concentration in a range of from about 0.005 microgram per 1 cm² to about 50 microgram per 1 cm² of wound area.

31. The composition of claim 23, wherein said heparanase has a concentration in a range of from about 0.5 microgram per 1 cm² to about 5 microgram per 1 cm² of wound area.

32. The composition of claim 23, wherein said heparanase is present in a concentration in a range of from about 10 micrograms to about 150 micrograms per dose.

33. A method of inducing or accelerating angiogenesis, the method comprising the step of administering a therapeutically effective amount of an isolated, purified, recombinant heparanase, so as to induce or accelerate angiogenesis.

34. The method of claim 33, wherein said heparanase is substantially free of contaminants.

35. The method of claim 33, wherein said recombinant heparanase includes a polypeptide having heparanase catalytic activity as set forth in SEQ ID Nos: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity.

36. The method of claim 33, wherein said recombinant heparanase includes a polypeptide having heparanase catalytic activity at least 60% homologous to SEQ ID NOs: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity, as determined with the Smith-Waterman algorithm, using the Bioaccelerator platform developed by Compugene (gapop equals 10.0, gapext equals 0.5, matrix: blosum 62).

37. The method of claim 33, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide as set forth in any of SEQ ID NOs: 9, 13, 42 or 43.

38. The method of claim 37, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide at least 60%

identical with SEQ ID NOs: 9, 13, 42 or 43 as determined using the Bestfit procedure of the DNA sequence analysis software package developed by the Genetic Computer Group (GCG) at the University of Wisconsin (gap creation penalty equals 12, gap extension penalty equals 4).

39. The method of claim 33, wherein said heparanase is contained in a pharmaceutical composition.

40. The method of claim 39, wherein said pharmaceutical composition is selected from the group consisting of an aqueous solution, a gel, a cream, a paste, a lotion, a spray, a suspension, a powder, a dispersion, a salve and an ointment.

41. The method of claim 39, wherein said pharmaceutical composition includes a solid support.

42. The method of claim 33, wherein said heparanase has a concentration in a range of from about 0.005 microgram per 1 cm² to about 50 microgram per 1 cm² of wound area.

43. The method of claim 42, wherein said heparanase has a concentration in a range of from about 0.5 microgram per 1 cm² to about 5 microgram per 1 cm² of wound area.

44. The method of claim 33, wherein said heparanase is present in a concentration in a range of from about 10 micrograms to about 150 micrograms per dose.

45. A pharmaceutical composition for inducing or accelerating angiogenesis, the pharmaceutical composition comprising, as an active ingredient, a therapeutically effective amount of an isolated, purified, recombinant heparanase, and a pharmaceutical carrier.

46. The composition of claim 45, packed and identified for treatment of inducing or accelerating angiogenesis.

47. The composition of claim 45, wherein said heparanase is substantially free of contaminants.

48. The composition of claim 45, wherein said recombinant heparanase includes a polypeptide having heparanase catalytic activity as set forth in SEQ ID Nos: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity.

49. The composition of claim 48, wherein said recombinant heparanase includes a polypeptide at least 60% homologous to SEQ ID NOs: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity, as determined with the Smith-Waterman algorithm, using the Bioaccelerator platform developed by Compugene (gapop equals 10.0, gapext equals 0.5, matrix: blosum 62).

50. The composition of claim 45, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide as set forth in any of SEQ ID NOs: 9, 13, 42 or 43.

51. The composition of claim 50, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide at least 60% identical with SEQ ID NOs: 9, 13, 42 or 43 as determined using the Bestfit

procedure of the DNA sequence analysis software package developed by the Genetic Computer Group (GCG) at the University of Wisconsin (gap creation penalty equals 12, gap extension penalty equals 4).

52. The composition of claim 45, wherein said pharmaceutical composition is selected from the group consisting of an aqueous solution, a gel, a cream, a paste, a lotion, a spray, a suspension, a powder, a dispersion, a salve and an ointment.

53. The composition of claim 52, wherein said pharmaceutical composition includes a solid support.

54. The composition of claim 45, wherein said heparanase has a concentration in a range of from about 0.005 microgram per 1 cm² to about 50 microgram per 1 cm² of wound area.

55. The composition of claim 45, wherein said heparanase has a concentration in a range of from about 0.5 microgram per 1 cm² to about 5 microgram per 1 cm² of wound area.

56. The composition of claim 45, wherein said heparanase is present in a concentration in a range of from about 10 micrograms to about 150 micrograms per dose.

57. An article of manufacture comprising packaging material and a therapeutically effective amount of an isolated, purified heparanase, wherein said packaging material comprises a label or package insert indicating that said heparanase can be administered to a human for inducing or accelerating a healing process of a wound.

58. The article of manufacture of claim 57, wherein said wound is selected from the group consisting of an ulcer, a burn, laceration, a surgical incision, necrosis and a pressure wound.

59. The article of manufacture of claim 58, wherein said ulcer is a diabetic ulcer.

60. The article of manufacture of claim 57, wherein said heparanase is substantially free of contaminants.

61. The article of manufacture of claim 57, wherein said heparanase is recombinant.

62. The article of manufacture of claim 61, wherein said recombinant heparanase includes a polypeptide having heparanase catalytic activity as set forth in SEQ ID Nos: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity.

63. The article of manufacture of claim 62, wherein said recombinant heparanase includes a polypeptide at least 60% homologous to SEQ ID NOs: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity, as determined with the Smith-Waterman algorithm, using the Bioaccelerator platform developed by Compugene (gapop equals 10.0, gapext equals 0.5, matrix: blosum 62).

64. The article of manufacture of claim 61, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide as set forth in any of SEQ ID NOs: 9, 13, 42 or 43.

65. The article of manufacture of claim 64, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide at least 60% identical with SEQ ID NOs: 9, 13, 42 or 43 as determined using the Bestfit procedure of the DNA sequence analysis software package developed by the Genetic Computer Group (GCG) at the University of Wisconsin (gap creation penalty equals 12, gap extension penalty equals 4).

66. The article of manufacture of claim 57, wherein said heparanase is contained in a pharmaceutical composition adapted for topical application.

67. The article of manufacture of claim 66, wherein said pharmaceutical composition is selected from the group consisting of an aqueous solution, a gel, a cream, a paste, a lotion, a spray, a suspension, a powder, a dispersion, a salve and an ointment.

68. The article of manufacture of claim 66, wherein said pharmaceutical composition includes a solid support.

69. The article of manufacture of claim 57, wherein said heparanase has a concentration in a range of from about 0.005 microgram per 1 cm² to about 50 microgram per 1 cm² of wound area.

70. The article of manufacture of claim 69, wherein said heparanase has a concentration in a range of from about 0.5 microgram per 1 cm² to about 5 microgram per 1 cm² of wound area.

71. The article of manufacture of claim 57, wherein said heparanase is present in a concentration in a range of from about 10 micrograms to about 150 micrograms per dose.

72. An article of manufacture comprising packaging material and a therapeutically effective amount of an isolated, purified heparanase, wherein said packaging material comprises a label or package insert indicating that said heparanase can be administered to a human for inducing or accelerating angiogenesis.

73. The article of manufacture of claim 72, wherein said heparanase is substantially free of contaminants.

74. The article of manufacture of claim 72, wherein said heparanase is recombinant.

75. The article of manufacture of claim 74, wherein said recombinant heparanase includes a polypeptide having heparanase catalytic activity as set forth in SEQ ID Nos: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity.

76. The article of manufacture of claim 75, wherein said recombinant heparanase includes a polypeptide at least 60% homologous to SEQ ID NOs: 10, 14, 44 or a fragment thereof having said heparanase catalytic activity, as determined with the Smith-Waterman algorithm, using the Bioaccelerator platform developed by Compugene (gapop equals 10.0, gapext equals 0.5, matrix: blosum 62).

77. The article of manufacture of claim 74, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide as set forth in any of SEQ ID NOs: 9, 13, 42 or 43.

78. The article of manufacture of claim 77, wherein said recombinant heparanase includes a polypeptide encoded by a polynucleotide at

least 60% identical with SEQ ID NOs: 9, 13, 42 or 43 as determined using the Bestfit procedure of the DNA sequence analysis software package developed by the Genetic Computer Group (GCG) at the University of Wisconsin (gap creation penalty equals 12, gap extension penalty equals 4).

79. The article of manufacture of claim 72, wherein said heparanase is contained in a pharmaceutical composition.

80. The article of manufacture of claim 79, wherein said pharmaceutical composition is selected from the group consisting of an aqueous solution, a gel, a cream, a paste, a lotion, a spray, a suspension, a powder, a dispersion, a salve and an ointment.

81. The article of manufacture of claim 79, wherein said pharmaceutical composition includes a solid support.

82. The article of manufacture of claim 72, wherein said heparanase has a concentration in a range of from about 0.005 microgram per 1 cm² to about 50 microgram per 1 cm² of wound area.

83. The article of manufacture of claim 82, wherein said heparanase has a concentration in a range of from about 0.5 microgram per 1 cm² to about 5 microgram per 1 cm² of wound area.

84. The article of manufacture of claim 72, wherein said heparanase is present in a concentration in a range of from about 10 micrograms to about 150 micrograms per dose.